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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	May 12	EXTEND option available in structure searching
NEWS	4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS	5	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS	6	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS	7	Jun 28	Additional enzyme-catalyzed reactions added to CASREACT
NEWS	8	Jun 28	ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R)
NEWS	9	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 15:05:21 ON 28 JUL 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:05:27 ON 28 JUL 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 JUL 2004 HIGHEST RN 717822-84-9
DICTIONARY FILE UPDATES: 27 JUL 2004 HIGHEST RN 717822-84-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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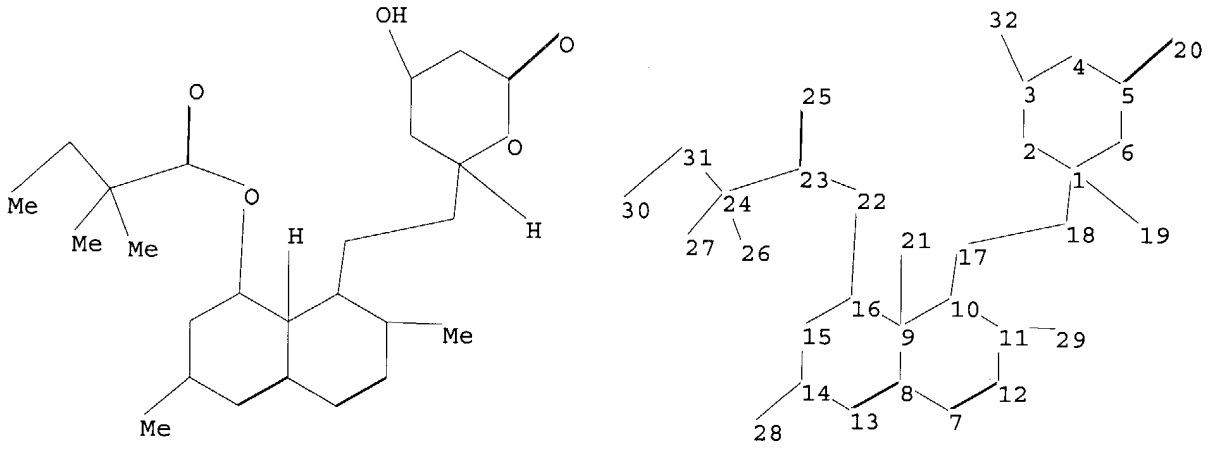

chain nodes :
17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
1-18 1-19 3-32 5-20 9-21 10-17 11-29 14-28 16-22 17-18 22-23 23-24
23-25 24-26 24-27 24-31 30-31
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 8-13 9-10 9-16 10-11 11-12 13-14
14-15 15-16
exact/norm bonds :
1-2 1-6 2-3 3-4 3-32 4-5 5-6 5-20 7-8 7-12 8-9 8-13 9-10 9-16 10-11
11-12 13-14 14-15 15-16 16-22 22-23 23-25
exact bonds :
1-18 1-19 9-21 10-17 11-29 14-28 17-18 23-24 24-26 24-27 24-31 30-31

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS

L1 STRUCTURE UPLOADED

=>
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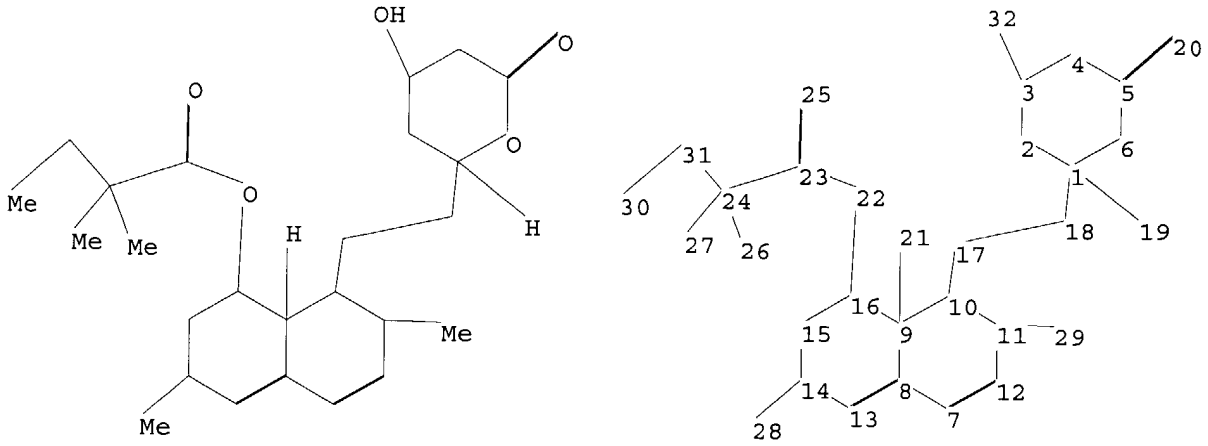

chain nodes :
17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
chain bonds :
1-18 1-19 3-32 5-20 9-21 10-17 11-29 14-28 16-22 17-18 22-23 23-24
23-25 24-26 24-27 24-31 30-31
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 8-13 9-10 9-16 10-11 11-12 13-14
14-15 15-16
exact/norm bonds :
3-32 5-20 16-22 22-23 23-25
exact bonds :
1-2 1-6 1-18 1-19 2-3 3-4 4-5 5-6 7-8 7-12 8-9 8-13 9-10 9-16 9-21
10-11 10-17 11-12 11-29 13-14 14-15 14-28 15-16 17-18 23-24 24-26 24-27
24-31 30-31
isolated ring systems :
containing 1 : 7 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS

L2 STRUCTURE UPLOADED

=> s l2
SAMPLE SEARCH INITIATED 15:06:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 18 TO ITERATE

100.0% PROCESSED 18 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 106 TO 614
PROJECTED ANSWERS: 3 TO 163

L3 3 SEA SSS SAM L2

=> s l2 ful
FULL SEARCH INITIATED 15:07:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 280 TO ITERATE

100.0% PROCESSED 280 ITERATIONS 28 ANSWERS
SEARCH TIME: 00.00.01

L4 28 SEA SSS FUL L2

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 156.26 156.47

FILE 'CAPLUS' ENTERED AT 15:07:15 ON 28 JUL 2004
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FILE COVERS 1907 - 28 Jul 2004 VOL 141 ISS 5
FILE LAST UPDATED: 27 Jul 2004 (20040727/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4
L5 2079 L4

=> s l4 and (process or make or made or prepar? or synthes?)
2079 L4
1958444 PROCESS
1299692 PROCESSES
2911574 PROCESS
(PROCESS OR PROCESSES)
192678 MAKE
148039 MAKES
331508 MAKE
(MAKE OR MAKES)

```
        1103437 MADE
             24 MADES
        1103457 MADE
                   (MADE OR MADES)
        1480947 PREPAR?
         110746 PREP
           1954 PREPS
         112505 PREP
                   (PREP OR PREPS)
        1874342 PREPD
             21 PREPDS
        1874357 PREPD
                   (PREPD OR PREPDS)
          97386 PREPG
             12 PREPGS
          97397 PREPG
                   (PREPG OR PREPGS)
        2490259 PREPN
         195592 PREPNS
        2638614 PREPN
                   (PREPN OR PREPNS)
        4367118 PREPAR?
                   (PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)
        1381870 SYNTHES?
L6          650 L4 AND (PROCESS OR MAKE OR MADE OR PREPAR? OR SYNTHES?)

=> s l6 and acetonitrile
          69863 ACETONITRILE
            964 ACETONITRILES
          70295 ACETONITRILE
                   (ACETONITRILE OR ACETONITRILES)
L7           13 L6 AND ACETONITRILE

=> s l6 and glacial acetic acid
          29919 GLACIAL
             72 GLACIALS
          29935 GLACIAL
                   (GLACIAL OR GLACIALS)
         204144 ACETIC
             22 ACETICS
         204153 ACETIC
                   (ACETIC OR ACETICS)
        3846720 ACID
        1439656 ACIDS
        4315045 ACID
                   (ACID OR ACIDS)
           3016 GLACIAL ACETIC ACID
                   (GLACIAL(W)ACETIC(W)ACID)
L8            2 L6 AND GLACIAL ACETIC ACID

=> dup rem l7 l8
PROCESSING COMPLETED FOR L7
PROCESSING COMPLETED FOR L8
L9           14 DUP REM L7 L8 (1 DUPLICATE REMOVED)

=> d l9 ibib hitstr abs 1-14

L9   ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:155665  CAPLUS
DOCUMENT NUMBER:          140:169718
```

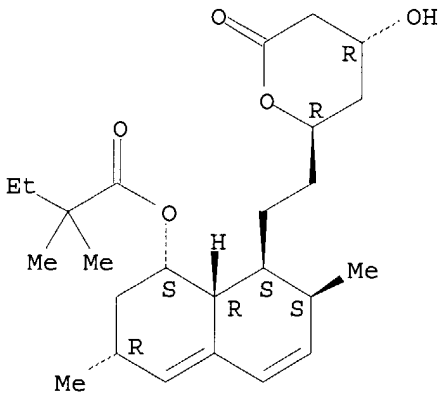
TITLE: Solid pharmaceutical formulation containing lovastatin and simvastatin
INVENTOR(S): Pflaum, Zlatko; Salobir, Mateja; Jerala, Zdenka; Resman, Aleksander
PATENT ASSIGNEE(S): Lek Pharmaceuticals D.D., Slovenia
SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6696086	B1	20040224	US 2000-657853	20000908
US 2004138295	A1	20040715	US 2003-742367	20031219

PRIORITY APPLN. INFO.: SI 1999-211 A 19990910
US 2000-657853 A1 20000908

IT **79902-63-9**, Simvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(solid pharmaceutical formulation containing lovastatin and simvastatin)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The present invention relates to a novel solid pharmaceutical formulation containing lovastatin and simvastatin, resp., with a particle size of 15-100 μm and a specific particle surface area of 1-4 m2/g, and to the **process** for its **preparation** The novel solid pharmaceutical formulation is useful for treating hypercholesterolemia and hyperlipidemia. Lovastatin (18.08 kg) was dissolved in 1080-L EtOAc and concentrated to the volume of 180 L. The resulting concentrate was cooled to 10°
and crystals were formed. The crystals formed were filtered and dried. A measured size of the formed lovastatin crystals was 163 μm, and a sp. surface area 0.7 m2/g.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:155656 CAPLUS

DOCUMENT NUMBER: 140:205215
TITLE: **Process** for obtaining HMG-CoA reductase inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): LEK Pharmaceuticals D.D., Slovenia
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6695969	B1	20040224	US 2001-720952	20010103
WO 2000017182	A1	20000330	WO 1999-IB1553	19990917

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2004138294	A1	20040715	US 2003-698009	20031030

PRIORITY APPLN. INFO.:

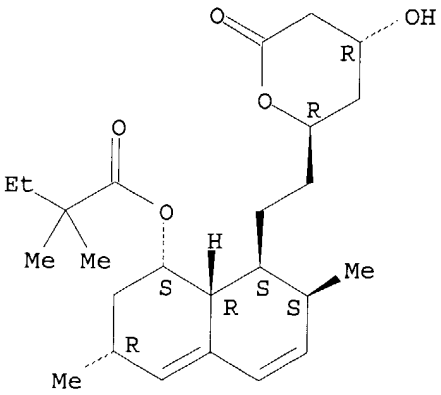
SI 1998-80241	A	19980918
WO 1999-IB1553	W	19990917
SI 1998-241	A	19980918
US 2001-720952	A2	20010103

IT **79902-63-9P**, Simvastatin
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(displacement chromatog. for obtaining HMG-CoA reductase inhibitors of high purity)

RN 79902-63-9 CAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs thereof are known as HMG-CoA reductase inhibitors and

are used as antihypercholesterolemic agents. The majority of them are produced by fermentation using microorganisms of different species identified as species belonging to Aspergilus, Monascus, Nocardia, Amycolatopsis, Mucor or Penicilium genus, some are obtained by treating the fermentation products using the method of chemical **synthesis** or they are the products of total chemical **synthesis.** The purity of the active ingredient is an important factor for manufacturing the safe and effective pharmaceutical, especially if the pharmaceutical product must be taken on a longer term basis in the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial **process** for the isolation of HMG-CoA reductase inhibitors using so-called displacement chromatog. Use of the invention enables to obtain HMG-CoA reductase inhibitors of high purity, with high yields, lower production costs and suitable ecol. balance.

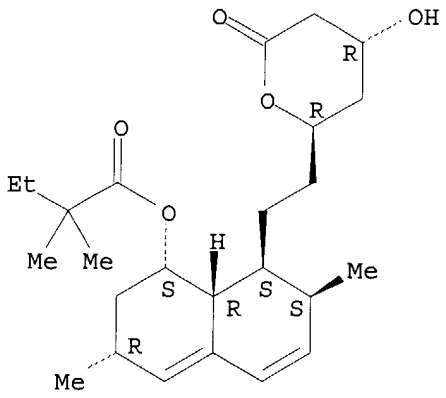
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:777774 CAPLUS
DOCUMENT NUMBER: 139:307681
TITLE: **Process** for the **preparation** of 4-oxytetrahydropyran-2-ones
INVENTOR(S): Zupancic, Silvo; Krasovec, Dusan; Zupet, Pavel
PATENT ASSIGNEE(S): Krka Tovarna Zdravil, D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080591	A1	20031002	WO 2003-SI9	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21187	C	20031031	SI 2002-86	20020326

PRIORITY APPLN. INFO.: SI 2002-86 A 20020326
OTHER SOURCE(S): CASREACT 139:307681; MARPAT 139:307681
IT **79902-63-9P**, Simvastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(manufacture from silylated simvastatin using triethylamine hydrochloride in organic solvents)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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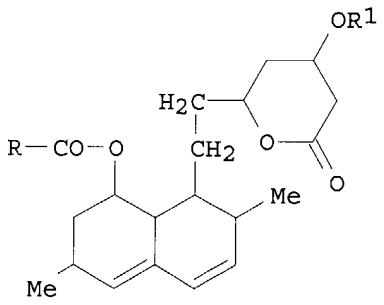

I

AB A **process** for the **preparation** of inhibitors of HMG-CoA reductase, such as simvastatin, from 4-silyloxytetrahydropyran-2-ones with NEt3.3HF being used as the desilylation reagent is described. The reaction was performed in organic solvents, a mixture thereof or without solvents. It is characteristic of this reaction that no addnl. impurities were obtained and that it takes place without the use of addnl. catalysts and with low excesses of the reagent.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:610206 CAPLUS
DOCUMENT NUMBER: 139:164542
TITLE: **Preparation** of cycloalkyl inhibitors of potassium channel function for preventing/treating arrhythmia and IKur-associated conditions
INVENTOR(S): Lloyd, John; Jeon, Yoon T.; Finlay, Heather; Yan, Lin; Gross, Michael F.; Beaudoin, Serge
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; Icagen, Inc.
SOURCE: PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063797	A2	20030807	WO 2003-US3170	20030131

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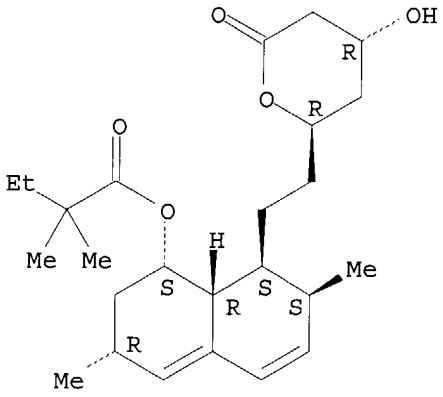
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

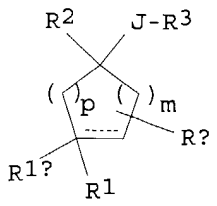
US 2004072880	A1	20040415	US 2003-356158	20030131

PRIORITY APPLN. INFO.: US 2002-353884P P 20020201
OTHER SOURCE(S): MARPAT 139:164542
IT **79902-63-9**, Simvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined with cycloalkyl inhibitors of potassium channel function for preventing/treating arrhythmia and IKur-associated conditions)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Claimed are novel cycloalkyl compds. (shown as I; variables defined below; e.g. cis- and trans-N-(4-hydroxy-1-thiophen-2-ylcyclohexylmethyl)-2-methoxybenzamide and trans-N-[[4-[N'-cyano-N''-ethyl-N-(furan-2-ylmethyl)guanidino]-1-phenylcyclohexyl]methyl]-2-methoxybenzamide) useful as inhibitors of K channel function (especially inhibitors of the Kv1 subfamily of voltage gated K+ channels, especially inhibitors Kv1.5 which was linked to the ultra-rapidly activating delayed rectifier K+ current IKur; no data), methods of using such compds. in the prevention and treatment of arrhythmia and IKur-associated conditions, and pharmaceutical compns. containing such compds. For I: dashed line = an optional double bond, provided that R1a is absent when a double bond is present; m and p = 0-3; R1 = H, NR8C(:W)NR6R7 (W = NR8a2, NCO2R8a2, NC(O)R8a2, NCN, NSO2R8a2), NR8SO2NR6R7, etc.; R1a = H, RX; or R1 and R1a together form oxo; or R1 and R1a together with the C atom to which they are attached combine to form an (un)substituted spiro-fused heterocyclo group; or R1 and R1a together combine to form :CR8R9. R2 is heteroaryl, (heteroaryl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, alkyl, alkenyl or cycloalkyl; J is a bond, C1-4 alkylene or C1-4 alkenylene; R3 = R5 (R5 = NR6aR7a, heteroaryl, (heteroaryl)alkyl, aryl, arylalkyl, alkyl, etc.), OR5, C(:Z1)R5, OC(:Z1)R5, C(:Z1)OR5, NR8a1C(:Z1)R5, etc.; RX is one or more optional substituents, attached to any available ring carbon atom; addnl. details including provisos are given in the claims. Although the methods of **preparation** are not claimed, >600 example **prepns**. are included.

L9 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:434162 CAPLUS
DOCUMENT NUMBER: 139:6712
TITLE: **Process** for **preparation** of lovastatin and simvastatin by lactonization
INVENTOR(S): Lee, Kwang-hyeg; Kim, Jin-wan; Choi, Kwang-do; Lee, Sang-ho; Cho, Hong-suk
PATENT ASSIGNEE(S): CJ Corporation, S. Korea
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

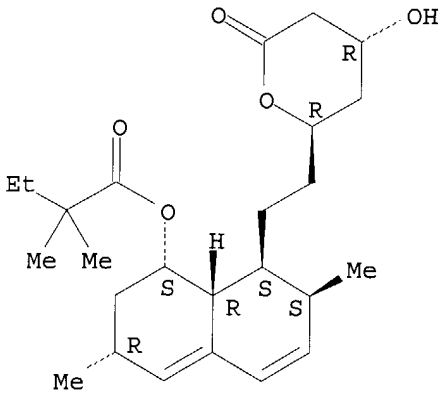
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1316552	A1	20030604	EP 2002-26916	20021203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2003048149	A1	20030612	WO 2002-KR2095	20021111
W: AE, AG, AL, AM, AT, AZ, BA, BB, BG, BY, BZ, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,				

IL, IN, IS, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003109723	A1	20030612	US 2002-295300	20021114
CN 1425661	A	20030625	CN 2002-153037	20021129
JP 2003183271	A2	20030703	JP 2002-350255	20021202
BR 2002004943	A	20040615	BR 2002-4943	20021202

PRIORITY APPLN. INFO.: KR 2001-75991 A 20011203
OTHER SOURCE(S): CASREACT 139:6712; MARPAT 139:6712
IT **79902-63-9P**, Simvastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(**process** for **preparation** of lovastatin and simvastatin by lactonization)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The present invention relates to a processing method for **preparing** lovastatin and simvastatin which comprises the steps of (1) performing lactonization of mevinic acid and its homologous compds. in the presence of a mixed organic solvent without an acid catalyst through nitrogen sweep; and (2) crystallization In the **process** lovastatin and simvastatin can be produced in a high yield with high purity and heterodimers formed as a byproduct can be reduced remarkably. Therefore, the processing method of the present invention can be convenient and economical.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

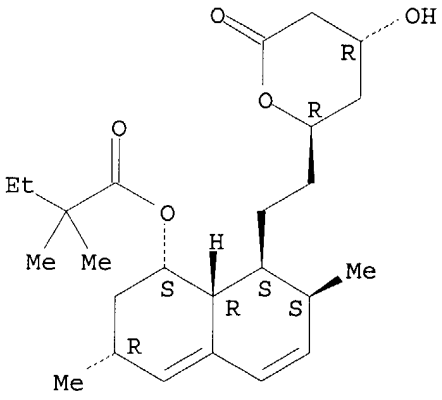
L9 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:172972 CAPLUS
DOCUMENT NUMBER: 138:221390
TITLE: **Process** of lactonization and crystallization in the **preparation** of highly purified statins
INVENTOR(S): Lee, Kwang-Hyeg; Kim, Jin-Wan; Yoon, Myeong-Sik; Choi, Kwang-Do; Lee, Sang-Ho; Cho, Hong-Suk
PATENT ASSIGNEE(S): Cheil Jedang Corporation, S. Korea
SOURCE: Eur. Pat. Appl., 11 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

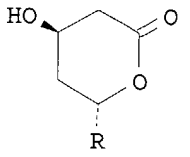
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288212	A1	20030305	EP 2002-15509	20020710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2003018570	A1	20030306	WO 2002-KR1281	20020706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003050482	A1	20030313	US 2002-200174	20020723
US 6649775	B2	20031118		
CN 1406938	A	20030402	CN 2002-127086	20020729
JP 2003096071	A2	20030403	JP 2002-245931	20020826

PRIORITY APPLN. INFO.: KR 2001-51796 A 20010827
OTHER SOURCE(S): CASREACT 138:221390; MARPAT 138:221390
IT **79902-63-9P**, Simvastatin
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of highly purified statins via lactonization of mevinic acid analogs and crystallization)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

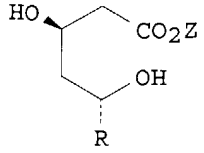
Absolute stereochemistry.



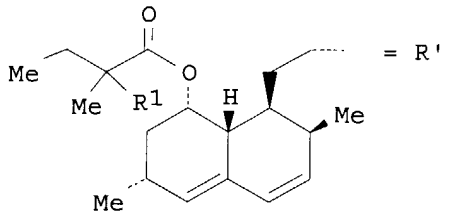
GI



I



II



AB The present invention relates to a **process** for **preparing** lovastatin (I; R = R', R1 = α-H) and simvastatin (I; R = R', R1 = Me) which comprises a step of (1) performing a lactonization of mevinic acid analogs II (Z = H, NH4, metal cation) in the presence of a dehydrating agent and without an acid catalyst under nitrogen sweep; and then a step of (2) making crystals at a high temperature In the **process** of the present invention, I can be produced highly purified in a high yield and, especially, heterodimers formed as a byproduct can be reduced in an amount remarkably. Therefore, the **process** of the present invention is convenient and economical.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:796454 CAPLUS
DOCUMENT NUMBER: 139:297013
TITLE: Drug microparticles deposited on sugar, starch, lactose, or cellulose carrier particles from solid solutions
INVENTOR(S): Lerner, Itzhak E.; Rosenberger, Vered; Flashner-Barak, Moshe; Drabkin, Anna; Moldavski, Naomi
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082247	A2	20031009	WO 2003-US9327	20030325
WO 2003082247	A3	20040205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,

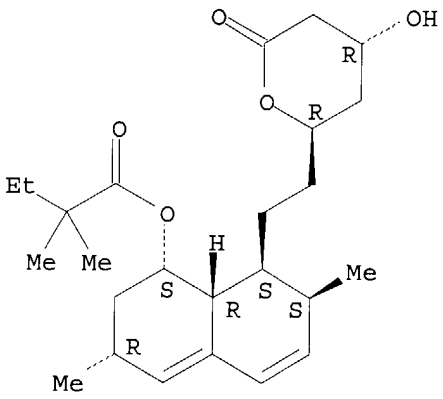
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003224059 A1 20031204 US 2003-400100 20030325
PRIORITY APPLN. INFO.: US 2002-367957P P 20020326

IT **79902-63-9**, Simvastatin
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(drug microparticles deposited on carrier particles from solid solution in sublimable carrier)

RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A drug delivery vehicle is provided including a pharmaceutical carrier particle, especially sugar, starch, lactose, or microcryst. cellulose particles, bearing microparticles of a drug, especially a drug with poor water solubility The microparticles of the drug are deposited on the pharmaceutical carrier particles from a solid solution of the drug in a sublimable carrier such as menthol, thymol, camphor, tert-butanol, trichloro-tert-butanol, imidazole, coumarin, **glacial acetic acid**, dimethylsulfone, urea, vanillin, camphene, salicylamide, and 2-aminopyridine. A method of making a drug delivery vehicle comprises the steps of (a) forming a solid solution of the drug and a sublimable carrier on the surface of a pharmaceutical carrier particle, and (b) subliming the sublimable carrier from the solid solution to deposit microparticles of the drug on the surface of the pharmaceutical carrier particle to obtain the drug delivery vehicle. The sublimable carrier is sublimed from the solid solution by treating the pharmaceutical carrier particles in a fluidized bed drier at a temperature below the m.p. of the solid solution For example, fenofibrate was dissolved in melted menthol, microcryst. cellulose was added to the melt, and the mass obtained was allowed to cool to room temperature and milled. The powder was transferred to a fluid bed dryer where the

menthol was removed and micronized fenofibrate deposited on microcryst. cellulose was obtained. Fenofibrate micronized by the methanol method gave 100% dissoln. in 2 h. The equivalent simple combination with microcryst. cellulose (control, not deposited from menthol) gave 40.2% dissoln. in 3 h, while a mech. micronized fenofibrate mixed with microcryst. cellulose gave 72.1% dissoln. in 3 h.

L9 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:906185 CAPLUS
DOCUMENT NUMBER: 137:384690
TITLE: **Preparation** of simvastatin from simvastatin acid derivs. via lactonization
INVENTOR(S): Ramesh, Dandala; Sonny, Sebastian; Dandala, Subramanyam; Meenakshisunderam, Sivakumaran
PATENT ASSIGNEE(S): Aurobindo Pharma Limited, India
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094803	A1	20021128	WO 2002-IN121	20020516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21234	C	20031231	SI 2002-20004	20020516
EP 1387835	A1	20040211	EP 2002-743614	20020516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004520444	T2	20040708	JP 2002-591476	20020516
BG 107477	A	20040130	BG 2003-107477	20030117
US 2004077884	A1	20040422	US 2003-602463	20030623

PRIORITY APPLN. INFO.: IN 2001-CH402 A 20010518
WO 2002-IN121 W 20020516

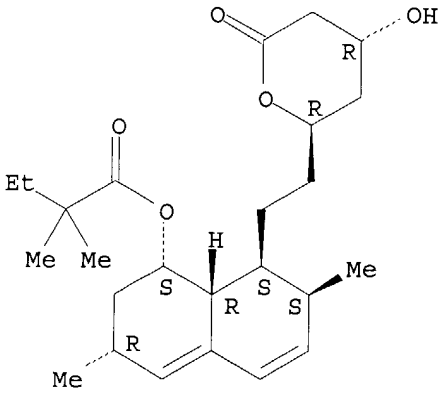
OTHER SOURCE(S): CASREACT 137:384690

IT **79902-63-9P**, Simvastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of simvastatin from simvastatin acid derivs. via lactonization)

RN 79902-63-9 CAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI

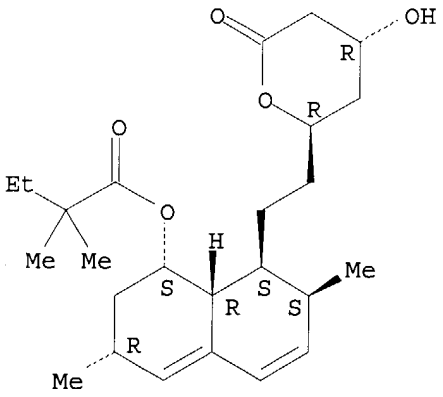
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses a **process** for **preparation** of simvastatin (I) from simvastatin acid derivs., such as II [Z = H, NH4], via lactonization. Thus, lactonization of II [Z = NH4], in a mixture of **acetonitrile** and glacial acetic acid to provide anhydrous conditions at a temperature of 65-70° C afforded I (yield = >97.4%) and a dimer impurity III (<0.1%).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:316903 CAPLUS
DOCUMENT NUMBER: 137:72249
TITLE: Effects of liquid chromatography mobile phase buffer contents on the ionization and fragmentation of analytes in liquid chromatographic/ionspray tandem mass spectrometric determination
AUTHOR(S): Zhao, Jamie J.; Yang, Amy Y.; Rogers, J. Douglas
CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Journal of Mass Spectrometry (2002), 37(4), 421-433
CODEN: JMSPFJ; ISSN: 1076-5174
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **79902-63-9**, Simvastatin
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(analyte; effects of liquid chromatog. mobile phase buffer contents on the ionization and fragmentation of analytes in liquid chromatog./ionspray tandem mass spectrometric determination)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The effects of liquid chromatog. mobile phase buffer contents on the ionization and fragmentation of drug mols. in liquid chromatog./ionspray tandem mass spectrometric (LC/MS/MS) determination were evaluated for simvastatin (SV) and its hydroxy acid (SVA). The objective was to improve further the sensitivity for SV by overcoming the unfavorable condition caused by the formation of multiple major adduct ions and multiple major fragment ions when using ammonium as LC mobile phase buffer. Mobile phases (70:30 **acetonitrile**-buffer, 2 mM, pH 4.5) with buffers **made** from ammonium, hydrazine or alkyl (Me, Et, di-Me or trimethyl)-substituted ammonium acetate were evaluated. Q1 scan and product ion scan spectra were obtained for SV in each of the mobile phases under optimized conditions. The results showed that, with the alkylammonium buffers, the alkylammonium-adducted SV was observed as the only major mol. ion, while the formation of other adduct ions ([M + H]+, [M + Na]+ and [M + K]+) was successfully suppressed. However, product ion spectra with a single major fragment ion were not observed for any of the alkylammonium-adducted SVs. The affinity of the alkylammoniums to SV and the basicity of the alkylamines are believed to be factors influencing the formation and abundance of mol. and fragment ions, resp. Methylammonium acetate provided the most favorable condition among all the buffers evaluated and improved the sensitivity several-fold for SV in LC/MS/MS quantitation compared with that obtained using ammonium acetate buffer. Better precision for SV in both Q1 and SRM scans was observed when using methylammonium buffer compared with those using ammonium buffer. The mobile phase buffer contents did not seem to affect the ionization, fragmentation and chromatog. of SVA. The results of this evaluation can be applied to similar situations with other organic mols. in ionspray LC/MS/MS determination

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:676761 CAPLUS
DOCUMENT NUMBER: 135:215976
TITLE: A **process** for purifying lovastatin and simvastatin with reduced levels of dimeric impurities
INVENTOR(S): Keri, Vilmos; Forgas, Ilona
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066538	A1	20010913	WO 2001-US6334	20010227
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002002288	A1	20020103	US 2001-793946	20010227
US 6521762	B2	20030218		
EP 1265884	A1	20021218	EP 2001-913139	20010227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003525935	T2	20030902	JP 2001-565354	20010227

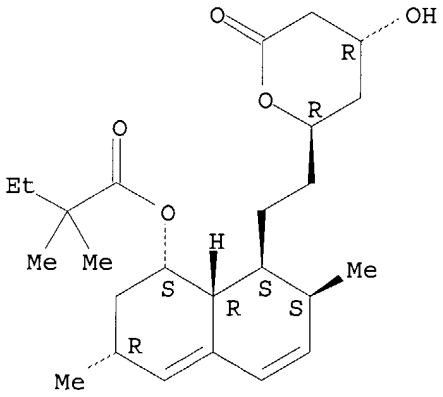
PRIORITY APPLN. INFO.: US 2000-186868P P 20000303
WO 2001-US6334 W 20010227

IT **79902-63-9P**, Simvastatin
RL: PUR (Purification or recovery); PREP (Preparation)
(mild base in alc. solvents for purifying lovastatin and simvastatin with reduced levels of dimeric impurities)

RN 79902-63-9 CAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Disclosed is a **process** for reducing the levels of dimeric impurities in a statin to less than 0.08 % by treatment of a statin containing more than 0.08 % dimeric impurities with a mild base in a suitable solvent mixture Lovastatin (in its lactone forms) was dissolved in a mixture of iso-Bu acetate and ethanol (3:1). This mixture was heated at 40-70° and concentrated NH4OH solution was added to the solution The mixture was cooled to give a product containing lovastatin dimer at ≤ 0.08 %.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

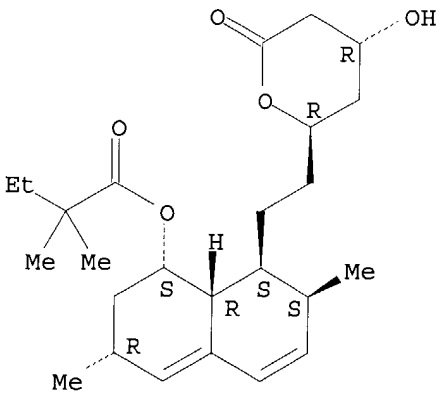
L9 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:319886 CAPLUS
DOCUMENT NUMBER: 134:328208
TITLE: Lactonization **process** for **preparation** of 3-hydroxylactone-containing products
INVENTOR(S): McManus, James; Anousis, Nicholas; Genus, John; Hancock, Christopher
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030773	A2	20010503	WO 2000-US29220	20001023
WO 2001030773	A3	20010614		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6380401	B1	20020430	US 2000-694190	20001023
EP 1228057	A2	20020807	EP 2000-971010	20001023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2002156298	A1	20021024	US 2002-117580	20020405
US 6525205	B2	20030225		

PRIORITY APPLN. INFO.: US 1999-161876P P 19991027
US 2000-694190 A3 20001023
WO 2000-US29220 W 20001023

OTHER SOURCE(S): MARPAT 134:328208
IT **79902-63-9P**, Simvastatin
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lactonization **process** for **preparation** of 3-hydroxylactone-containing products)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Crystalline 3-hydroxylactone-containing products can be **prepared** in high yield and purity in a one-pot **process** by treating the corresponding 3,5-dihydroxy acid with a strong mineral acid in a cold, aprotic, and water-miscible solvent to effect lactonization, followed by addition of excess acid to effect crystallization of the lactonized product from the reaction mixture The **process** is useful in making 3-hydroxy-3-methylglutaryl CoA reductase inhibitors, such as simvatatin.

L9 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:210141 CAPLUS
DOCUMENT NUMBER: 132:241979
TITLE: **Process** for obtaining HMG-CoA reductase inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017182	A1	20000330	WO 1999-IB1553	19990917
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SI 20072	C	20000430	SI 1998-241	19980918
CA 2343645	AA	20000330	CA 1999-2343645	19990917
AU 9955284	A1	20000410	AU 1999-55284	19990917
AU 766630	B2	20031023		
EP 1114040	A1	20010711	EP 1999-941797	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002526486	T2	20020820	JP 2000-574092	19990917

NZ 509582	A	20031031	NZ 1999-509582	19990917
US 6695969	B1	20040224	US 2001-720952	20010103
HR 2001000045	A1	20011231	HR 2001-45	20010116
BG 105348	A	20011130	BG 2001-105348	20010316
US 2004138294	A1	20040715	US 2003-698009	20031030

PRIORITY APPLN. INFO.:

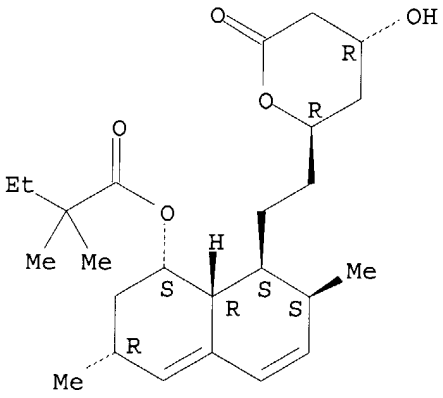
SI 1998-241	A	19980918
SI 1998-80241	A	19980918
WO 1999-IB1553	W	19990917
US 2001-720952	A2	20010103

IT **79902-63-9P**, Simvastatin
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**process** for obtaining HMG-CoA reductase inhibitors of high purity)

RN 79902-63-9 CAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs are known as HMG-CoA reductase inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermentation using microorganisms of different species identified as species belonging to Aspergillus, Monascus, Nocardia, Amycolatopsis, Mucor or Penicillium genus, some are obtained by treating the fermentation products using the method of chemical **synthesis** or they are the products of total chemical **synthesis.** The purity of the active ingredient is an important factor for manufacturing the safe and effective pharmaceutical, especially if the pharmaceutical product must be taken on a longer term basis in the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial **process** for the isolation of HMG-CoA reductase inhibitors using so-called displacement chromatog. Use of the invention enables to obtain HMG-CoA reductase inhibitors of high purity, with high yields, lower production costs and suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity 88%) was dissolved in the mobile phase A (distilled water), pH was adjusted to 7 with 0.2M aqueous NaOH solution and filtered. The column was equilibrated with mobile phase A. The sample

obtained in the above manner was fed onto the Grom-Sil 120-ODS HE column (particle size 30 11 μm, column size 250 x 10 mm). The column was washed with the mobile phase B containing 7% of diethylene glycol monobutyl ether in mobile phase A at the flow rate of 4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions were collected with an initial increase in the absorbance. When the signal decreased the column was washed with 25 mL of 70% MeOH. The fractions obtained were analyzed by the HPLC method. The fractions with a purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity was 99.8%.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

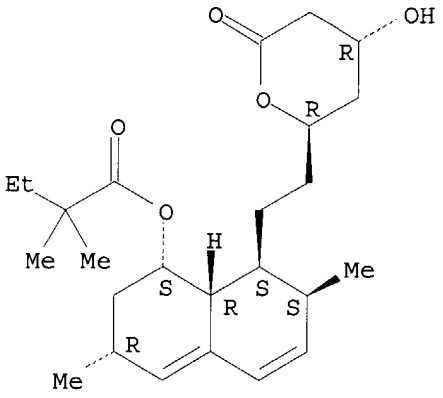
L9 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:658210 CAPLUS
DOCUMENT NUMBER: 117:258210
TITLE: Purification of lovastatin and related compounds for pharmaceutical use
INVENTOR(S): Haytko, Peter N.; Wildman, Arthur S., Jr.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9216276	A1	19921001	WO 1992-US1864	19920309
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5202029	A	19930413	US 1991-668831	19910313
CA 2104232	AA	19920914	CA 1992-2104232	19920309
EP 578723	A1	19940119	EP 1992-908427	19920309
EP 578723	B1	19990609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06506210	T2	19940714	JP 1992-508303	19920309
AT 180986	E	19990615	AT 1992-908427	19920309
ES 2132121	T3	19990816	ES 1992-908427	19920309

PRIORITY APPLN. INFO.: US 1991-668831 19910313
WO 1992-US1864 19920309

IT **79902-63-9**, Simvastatin
RL: BIOL (Biological study)
(purification for pharmaceutical use of, by HPLC)
RN 79902-63-9 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



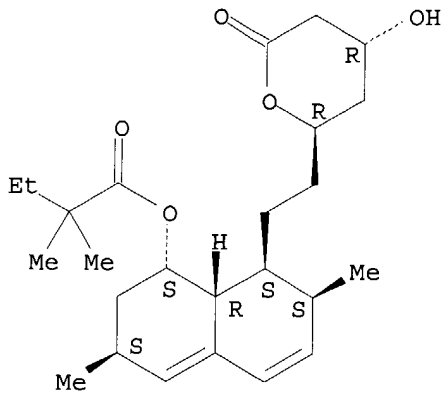
AB Crude **prepns.** of lovastatin and related inhibitors of hydroxymethylglutaryl CoA reductase are purified to a degree suitable for pharmaceutical use by HPLC or reverse-phase HPLC. Preferred column packings are silicas, activated C, and silanes. Crude lovastatin 4.6 g in 70% **acetonitrile** 200 mL was passed over a column (5+25 cm) of an irregular octadecylsilane (RG1010-C18) at 150 mL/min. The fraction eluting at K' = 2.0-3.0 was concentrated and crystallized to give lovastatin 99.7% in a yield of 90%.

L9 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:6341 CAPLUS
DOCUMENT NUMBER: 116:6341
TITLE: Desilylation of a 4-silyloxytetrahydropyran-2-one
INVENTOR(S): Decamp, Ann E.; Kawaguchi, Alan T.; Volante, Ralph P.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 444888	A1	19910904	EP 1991-301556	19910226
EP 444888	B1	19950208		
R: CH, DE, FR, GB, IT, LI, NL				
CA 2036962	AA	19910827	CA 1991-2036962	19910225
CA 2036962	C	19980915		
JP 04211679	A2	19920803	JP 1991-30866	19910226
US 5650523	A	19970722	US 1991-696449	19910506

PRIORITY APPLN. INFO.: US 1990-484332 19900226
OTHER SOURCE(S): CASREACT 116:6341; MARPAT 116:6341
IT **123049-81-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**preparation** of)
RN 123049-81-0 CAPLUS
CN Butanoic acid, 2,2-dimethyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1α,3β,7β,8β(2S*,4S*),8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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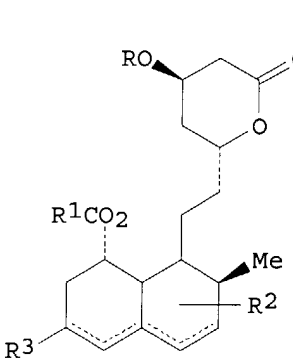

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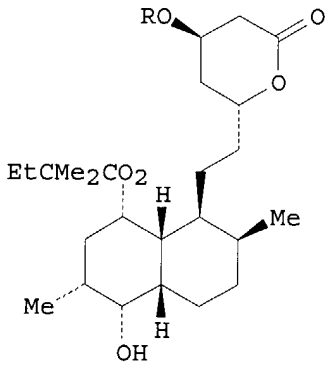

II

AB Title compds., especially I (R = trisubstituted silyl; R1 = alkyl; R2 = H, alkyl, OH, O, hydroxyalkyl; R3 = H, alkyl, hydroxyalkyl; the dotted bonds are single or double bonds), are desilylated by treatment with BF3.Et2O in MeCN, CH2Cl2, THF or AcOEt. Thus, II (R = SiMe2CMe3) was treated with BF3.Et2O in MeCN to give 87% II (R = H).

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	89.01	245.48
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.29	-10.29

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